

REMARKS

Reconsideration and allowance are respectfully requested.

Claims 21, 25, 27-31, 35 and 37-48 are pending. Non-elected claims 31-40 were withdrawn from consideration by the Examiner.

The amendments are fully supported by the original disclosure and, thus, no new matter is added by their entry. Support for the more precisely recited pH ranges may be found at page 28, line 22, to page 29, line 2, of the specification.

In claim 21, the β 1,3-N-acetyl-D-galactosamine transferase is described by high stringency hybridization and wash conditions using specific nucleotide sequences. It also recites the pH range of exemplary buffers as follows: MES buffer, sodium cacodylate buffer and HEPES buffer.

Claims 28-29 were objected to as allegedly substantial duplicates of each other. They are amended to specify their differences. Withdrawal of the objection is requested.

35 U.S.C. 112 – Enablement

The Patent Office has the initial burden to question the enablement provided for the claimed invention. M.P.E.P. § 2164.04, and the cases cited therein. It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 169 USPQ 367, 370 (C.C.P.A. 1971). Specific technical reasons are always required. See M.P.E.P. § 2164.04.

Claims 21, 24, 26 and 28-30 were rejected under Section 112, first paragraph, because it was alleged that the specification “does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with the claims.” Applicants traverse.

As noted above, Claim 21 is amended to recite high stringency hybridization and wash conditions using specific nucleotide sequences for the β ,3-N-acetyl-D-galactosamine transferase. Since this rejection is not applied to the claims 25 and 27, Applicants submit that the rejection should be withdrawn after entry of the amendment.

Withdrawal of the enablement rejection is requested because it would not require undue experimentation for a person of skill in the art to make/use the claimed invention.

35 U.S.C. 103 – Nonobviousness

To establish a case of prima facie obviousness, all of the claim limitations must be taught or suggested by the prior art. See M.P.E.P. § 2143.03. A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing the legal standard provided in *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See *id.* ("Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue"). The use of hindsight reasoning is impermissible. See *id.* at 1397 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning"). Thus, an obviousness rejection requires "some rationale, articulation, or reasoned basis to explain why the conclusion of obviousness is correct." *Kahn*, 78 USPQ2d at 1335; see *KSR*, 82 USPQ2d at 1396. Moreover, a claim which is directed to a combination of prior art elements "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id.* at 1396. Finally, a determination of prima facie obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claims 21-30 were rejected under Section 103(a) as allegedly unpatentable over Strausberg et al. (Proc. Natl. Acad. Sci. USA 99:16899-16903, 2002) or Kawai et al. (Nature 409:685-690, 2001) in view of Wandall et al. (J. Biol. Chem. 272:23503-23514, 1997). Applicants traverse.

Claims 21 and 28-29 are amended to specify the pH range of the following specific buffers: MES buffer, sodium cacodylate buffer, and HEPES buffer. All of Wandall's assays were performed with enzyme in a Tris (pH 7.4) buffer. Applicants' claimed invention requires specific buffers, which do not include a Tris (pH 7.4) buffer, and neither a suggestion or a reasonable expectation of success is found in the prior art to use "a buffer with a pH of at least 5.50 to 5.78 in MES buffer, a pH of around 5.0 in sodium cacodylate buffer, or a pH of around 7.4 to 7.5 in HEPES buffer" as required by the pending claims.

Applicants' specification, especially the working examples therein, makes clear that it would be nonobvious to determine buffer and pH conditions for an enzyme to act. Wandall discloses an enzyme that transfers a sugar to a peptide with alpha bond. But Applicants' enzyme transfers a sugar to a sugar chain as an acceptor substrate. Thus, Wandall's enzyme is quite different from Applicants' enzyme, and there would have been no reasonable expectation of success to extrapolate from the former's conditions to those recited in the pending claims. Therefore, one of ordinary skill in the art would not have found it obvious to come up with Applicants' claimed invention from Wandall.

Moreover, Applicants' claimed invention relates to a solution comprised of an enzyme transferring N-acetyl-D-galactosamine to N-acetyl-D-glucosamine with β 1,3 linkage. Neither Strausberg nor Kawai, however, discloses that their enzymes transfer N-acetyl-D-galactosamine to N-acetyl-D-glucosamine with β 1,3 linkage. When the claimed invention was made, "[I]t cannot be said that sufficient headway has been made in analyzing in vivo sugar chain synthesis. This is in part because the mechanism of sugar chain synthesis and the in vivo localization of sugar synthesis have not been fully analyzed" (page 2, lines 1-5, of Applicants' specification). Glycosylation enzymes are almost annotated with a galactosyltransferase in the prior art. In such a situation, surprisingly, Applicants found that the enzyme of the present invention has a transferase activity of N-acetyl galactosamine.

Furthermore, when the claimed invention was made, "Although there is a report showing that the sugar chain structure in which GalNAc and GlcNAc are linked in a β 1,3 fashion was confirmed in sugar chains on neutral glycolipids of fly, a kind of arthropod

(Non-patent Document 5), it has been believed that such a sugar chain structure is not present in mammals, particularly in humans, to begin with" (page 2, line 27, to page 3, line 5, of Applicants' specification). Thus, when the claimed invention was made, such a sugar chain structure had not been known to be present in humans. By contrast, Applicants' for the first time taught the enzyme of their invention could synthesize a novel sugar chain structure, GalNAc β 1-3GlcNAc, in humans. It is also well known that there is a lack of predictability in specifying enzyme conditions such as pH in the art when the only information available is the amino acid sequence. Therefore, one of ordinary skill in the art would not have found the enzyme solution of the claimed invention to be obvious from the amino acid sequences disclosed by Strausberg and Kawai. No known enzyme could synthesize the sugar having such a sugar chain. Therefore, Applicants' claimed invention differs from the prior art and permits elucidating of biological function of the novel sugars having this structure.

Withdrawal of the obviousness rejection is requested because the claimed invention would not have been obvious to the ordinarily skilled artisan at the time Applicants made their invention.

Conclusion

Having fully responded to all of the pending objections and rejections contained in this Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: /Gary R. Tanigawa/
Gary R. Tanigawa
Reg. No. 43,180

901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100